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14. ABSTRACT

At the end of study year 4 we completed all expected enrollment, intervention, and data collection as per our protocol. All necessary IRB approvals were obtained, and all regulatory documents submitted including the annual IRB continuing review, attached to this report (Shepherd IRB and University Maryland). All study personnel hold current certifications in order to participate in research. Multiple meetings occurred, both in person (at ASIA conference in San Antonio, May 2014) and via monthly teleconferencing in order to coordinate activities between the Baltimore and the Atlanta sites. Thirty seven research participants initiated the study (with 6 drop outs) by the September 30, 2014 end of enrollment date. Screening data entry and analysis is initiated and we eagerly examining our outcome data. Two manuscripts are published 9 presentations (platform and poster) occurred from our study proposal and screening data analysis to date.

15. SUBJECT TERMS

Motor Incomplete Spinal Cord Injury, Lokomat, Aquatic Therapy, Functional and Physiological Outcomes

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INTRODUCTION

The goal of this research was to compare the effects of three months, three times a week aquatic therapy with similar intensity robotically assisted, body weight supported aerobic treadmill training upon functional ambulatory ability, cardiovascular fitness, and metabolic changes in individuals with chronic (greater than 12 months post injury) motor incomplete spinal cord injury (MISCI). Thirty-seven individuals with chronic MISCI enrolled in this study. We hypothesized aquatic therapy would be more effective than robotically assisted aerobic locomotor training in improving functional ability as measured by timed walks, a gait mat device and community step activity monitors. Furthermore, we also hypothesized aquatic therapy would be more effective than robotic locomotor therapy in improving cardiovascular fitness as measured by open circuit spirometry during arm ergometry for these same participants. This work will provide preliminary evidence-based information as to the efficacy of aquatic therapy and robotically assisted, body weight supported aerobic treadmill training in chronic spinal cord injury motor system rehabilitation. A need for empirical data exists, as there is little objective data examining either of these two interventions after spinal cord injury.

BODY

Statement of Work (SOW) Tasks are listed below, and are followed (in blue and bold font) with description of the actual accomplishments during this annual study period.

Task 1: Implement plans, obtain IRB study approval and start up. . Complete the formal study protocol, case report forms, data collection sheets, and informed consent documents.

1a. Ensure consistency in these documents across the two sites.

1b. Annually submit the protocol and regulatory documents to the University of Maryland at Baltimore and the Shepherd Center IRBs.

1c. Maintain research certification for all study personnel, renewing as required.

1d. Continue regular meetings phone and face to face allowing for coordination of the research study and efficient dissemination of study results.

All these tasks were completed successfully. We did request and receive approval for a no cost extension to insure thorough data analysis. (please see attached letter). One more quarterly report (Dec 31, 2014) and the final study report (March 31, 2014) will be provided.

Task 2: Implement Randomized Clinical Trial (Months 7-42)

2a. Initiate screening of potential individuals for the research study (General medical and ASIA examination, blood tests, EKG, Standing frame challenge) (Months 7-9)

2b. Obtain baseline measurements (VO_2max, Timed walked tests, GAITRite, Step activity monitor studies) on individual study participants as they pass screening.

2c. Initiate the stratified randomization of subjects into the Lokomat versus aquatic therapy protocols with exercise occurring 3 times per week for 3 months. (Months 7 -9)
2d. Recruit twelve individuals across both sites during year one (approximately six per site approximately equally divided between tetraplegic and paraplegic individuals (Months 7-19).
2e Obtain 3 month outcome measurements after participants complete their first exercise intervention (Months 10-39).
2f. Cross over participants to the other exercise intervention after outcome measurements have been performed (Months 10-42).
2g. Obtain 6 month outcome measurements after participants complete their second exercise interventions (Months 12-42).

31 individuals were screened in Baltimore with 27 progressing to study participation and five individuals dropping out of the study. Three potential participants failed to meet screening criteria and one potential participant deferred secondary to an orthopedic issue which required attention. Fifteen individuals were screened and enrolled in Atlanta at Shepherd Center with fourteen progressing to study completion. At the end of this final reporting year, 31 participants completed the final data collection.

Task 3. Implement Analysis of Data, Presentation and Publication (Months12-45).
3a. Provide annual reports to the Data Safety Monitoring Board at the Baltimore site (Months 12-36).
3b. Complete proposed statistical analysis of the study data and submit the results for scholarly presentation and publication. In addition provide outcome information in the form of a report to the granting agency. (Months 36-45).

3a. The eighth DSMB report was submitted November 2014. The preceding seven DSMB reviews were positive, and we anticipate no issues with the eighth DSMB report as all participant involvement ended before this review period initiated. University of Maryland Baltimore and the Shepherd Center IRB annual reviews are attached to this document with no issues reported. 3b. Data analysis is not yet completed; however, two publications and nine study related presentations were completed to date.

Presentations:
Relationships among Physical Activity Scale for Individuals with Physical Disability (PASIPD), Body Mass Index (BMI), and Peak Oxygen Consumption (V02peak) in Persons with Motor Incomplete SCI. Presented at:

1) Both as Best Neurological Research Presentation and poster at American Academy of Physical Medicine and Rehabilitation, Washington DC, October 2013.

2) ASIA conference Chicago, IL, April 2013

3) Baltimore VA Research Day April 2013

4) Accepted for Combined Sections Meeting, American Physical Therapy Association, February 2014

Atypical Autonomic Dysreflexia during Robotically Assisted Body Weight Supported Treadmill Training in an Individual with Motor Incomplete Spinal Cord Injury. Presented at

1) ASIA conference Chicago, IL, April 2013

2) Baltimore VA Research Day April 2013

3) Accepted for Combined Sections Meeting, American Physical Therapy Association, February 2014

Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Treadmill Training.

1) Platform presentation by Peter Gorman MD: American Spinal Cord Professionals Annual Conference, Las Vegas, NV, Sept 2012.

2) Invited Healthcare Presentation by Paula Richley Geigle PT PhD: Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Treadmill Training. World Aquatic Health Conference: Norfolk, VA, October 2012.

Manuscripts

1) Geigle P, Frye S, Perreault J, Scott W, Gorman P. Atypical Autonomic Dysreflexia during Robotically Assisted Body Weight Supported Treadmill Training in an Individual with Motor Incomplete Spinal Cord Injury. *J Spinal Cord Medicine*. 36(2): 153-156 (2013).
2) Gorman PH, Geigle PT, York H, Scott W. Reliability and Relatedness of Peak VO2 Assessments during Body Weight Supported Treadmill Training and Arm Cycle Ergometry in Individuals with Chronic Motor Incomplete Spinal Cord Injury. In press, *Spinal Cord*.

Prose Summary Description of Recruitment Accomplishments:

The first Baltimore recruitment actually started in April 2011. Since then 31 individuals were screened with 27 progressing to study participation. Atlanta study recruitment began in July 2011 with 15 individuals screened and engaged in study participation. Recruitment at both sites began as soon as the Department of Defense (DOD) IRB review was complete. In Baltimore 17

participants and at Shepherd 14 participants completed the entire study. Demographic breakdown for all screened individuals includes the following:

Status key: I=first exercise arm, II=second exercise arm

Site key: 1=Baltimore, 2=Atlanta

Gender	Race/Ethnicity	Veteran	Age	Level	Status	Site
M	AA	no	41	C7	withdrawn-II	1
M	Asian	no	20	C5	withdrawn--I	1
F	Caucasian	no	48	T9	completed	1
M	Caucasian	no	36	T6	Screen failure: Open skin lesions	1
F	AA	no	28	T12	Screen failure: ASIA B	1
M	Caucasian	no	60	C5-6	completed	1
M	Caucasian	no	61	C5-6	completed	1
M	AA	yes	61	C4	completed	1
M	Caucasian	no	41	T1	withdrawn--I	1
M	Caucasian	yes	35	C4	completed	1
M	AA	no	51	T1	deferred start	1
M	AA	yes	65	L2	screen failure	1
M	Caucasian	no	51	C4	completed	1
F	Caucasian	no	44	T10	Withdrew -II	1

M	AA	no	27	T1	withdrawn-I	1
M	Am Indian	yes	49	C8	completed	1
M	Caucasian	no	46	C4	completed	1
M	Caucasian	no	55	T1	completed	1
F	Caucasian	no	30	C7	completed	1
F	AA	no	53	C3	completed	1
M	AA	yes	48	C8	completed	1
F	Islander	no	65	T1	completed	1
M	Hispanic	no	46	C4	completed	1
F	Caucasian	no	58	T1	completed	1
M	AA	no	57	T7	screen failure	1
M	AA	no	27	C6	completed	1
M	Caucasian	no	32	C8	completed	1
F	Caucasian	no	54	T3	completed	2
M	Caucasian	no	39	C5	completed	2
M	Caucasian	no	60	C4	completed	2
M	Caucasian	no	37	T8	completed	2
F	Caucasian	no	27	T1	completed	2
M	Caucasian	yes	65	C2	completed	2
M	AA	no	41	T6	completed	2
M	AA	no	50	C2	completed	2
F	Caucasian	no	25	C4	completed	2

M	Caucasian	no	31	C4	completed	2
M	Caucasian	no	40	T4	completed	2
M	AA	no	50	C2	enrolled-II	2
M	AA	no	39	C2	enrolled-II	2
M	Caucasian	no	51	C1	enrolled-I	2
F	AA	no	47	C4	withdrawn bowel program, HTN	2

Participants who were withdrawn:

Five individuals at the Baltimore site where withdrawn from study participation. One enrolled participant (at the Baltimore site) was withdrawn at his fourth training Lokomat exercise session secondary to his inability to tolerate Lokomat setup. Specifically, the fourth and final session was terminated during the warm-up period after the participant reported experiencing a "burning" sensation in the left foot. This participant reported similar symptoms during the two prior Lokomat training sessions but he did not report this symptom to the research team during the set-up and acclimation sessions. The reported paresthesia was not in a classical neuroanatomic distribution. For two of the last four attempted training sessions the participant actually reported paresthesia before leaving the exercise mat and being suspended in the Lokomat harness. To diminish or prevent this problem, the research team attempted to reposition the Lokomat straps, but was unsuccessful in ameliorating the condition during Lokomat suspension. The PI ultimately terminated the subject's participation for safety reasons.

The second participant was withdrawn on his 11th Lokomat session (after he completed the entire Aquatic therapy arm of the study with no problems) when asymptomatic autonomic dysreflexia (AD) occurred. This was detected after the participant described a 'feeling of warmth' while exercising on the Lokomat. The blood pressure taken at the time was 210/100 mmHg. The subject was otherwise asymptomatic, i.e. there was no headache or diaphoresis. The blood pressure returned to normal after the subject was taken out of the Lokomat straps. Several attempts were made to modify the straps to see if this elevation in BP could be avoided. Unfortunately it could not.

Autonomic dysreflexia is a known complication of persons with spinal cord injury at or above the T6 level, usually caused by some sensory irritation below the level of injury. We discussed this incident with the IRB at the time it occurred. Since AD is a known complication, no reportable new information (RNI) report was required. Because of the persistent elevation in BP during the Lokomat component of the protocol (i.e. silent AD), this individual was withdrawn from the study.

An unfortunate non-study activity related, lower leg fracture necessitated withdrawal of the third participant. He was casted for 6 weeks sp fracture.

An unreported skin irritation on the plantar surface of his foot facilitated the removal of the fourth research participant. This individual does not routinely examine his skin integrity, or follow up with recommended and scheduled clinical care. Once the irritation was researcher identified, the area was examined and treated until the participant no longer returned to our facility. Attempts were made to contact him via phone and mail with no success.

The fifth participant successfully completed the aquatic intervention and 30 sessions of Lokomat and was hospitalized for a non-study condition. One participant was withdrawn in Atlanta after 1 week of study involvement for medical conditions prohibiting ongoing study participation. She was referred to services to address these medical conditions.

All of these withdrawn individuals but the fifth who was directly admitted to the hospital from home, were medically evaluated by the PI (PHG) who determined that no further intervention was necessary other than withdrawal from participation. Two withdrawn individuals are currently engaged in our wellness aquatic programs as a secondary outcome of study participation. We diligently monitored all study participants to insure safe participation in this DOD protocol. Additionally, study withdraws were reported through our established DSMB.

KEY RESEARCH ACCOMPLISHMENTS

- At the 2014 ASIA Meeting, members of the University of Maryland Department of Neurology and UM Rehabilitation Research Center presented the following which was indirectly related to our DOD award as we highlighted much of our study aquatic protocol intervention:

  Paula Richley Geigle PT PhD, and **Sara Kate Frye OTR/L, MS**, presented a two part course: Aquatic Exercise for Individuals with Spinal Cord Dysfunction: Clinical Guidelines, didactic and in-pool experiences.

  John Perreault CRNP, William H. Scott MA, Peter Gorman MD, and Paula Richley Geigle PT, PhD Adjunct Assistant Professor presented: Gastric Sleeve Surgery in a Person with Chronic Motor Incomplete Tetraplegia: A Clinical Case Report. (poster presentation)

William H. Scott MA, Peter Gorman MD, John Perreault CRNP, Peter Kuchonov PhD, Paula Richley Geigle PT PhD, presented: Abdominal Adiposity, Insulin Resistance, and Prescribed Exercise for a Woman with Chronic Motor Incomplete Spinal Cord Injury: A Clinical Case Report. (platform presentation)

- Study protocol, case report forms, data collection sheets, and informed consent documents were maintained in a consistent manner across both study sites
- Filed all required regulatory documents for 4 years of study enrollment and intervention
- Obtained/maintained research certification for all study personnel

Orchestrated organizational face to face meetings in Baltimore, Atlanta, and at national professional meetings to allow for efficient coordination of the research study

- Held weekly DOD research study meetings (in Baltimore) including all local team members
- Planned and executed monthly phone conferencing between both study
- sites

Submitted local IRB modification to clarify exclusion criteria so that they better align with the current clinical definition of diabetes; and to offer optional participation in MRI screening at pre, mid, and post data assessment for abdominal adiposity.

- Two manuscripts from screening data and study execution only
- Nine presentations from proposal, screening data, and study execution only.

- The majority of our team members from both University Maryland Rehabilitation and Shepherd Center were present and met together at the American Spinal Injury Association (ASIA) annual meeting, San Antonio, TX, May 2014. We discussed specific details of the data analysis plan. Also at this meeting we were fortunate to meet Dr. Patricia Henry our Science Officer for this award.

Our plan for the 6 month no cost extension:

- Continue to provide quarterly and final study reports to the DOD and study closure documentation to UMB and Shepherd IRB.

- Submitted our eighth DSMB report in November 2014 which did not include any new participant information as all intervention and outcome collection was completed
- Analyze both screening and outcome data
- Draft publication(s) discussing: clinical concepts; cardiovascular; functional; and metabolic information acquired from this DOD funded study
- Draft a final study report for DOD and study closure reports for both UM and Shepherd

REPORTABLE OUTCOMES: No reportable outcomes available to date.

CONCLUSION: At the conclusion of year 4 of the DOD study we met all planned proposal activities: regulatory compliance, recruitment, data collection, and fiscal responsibility; and are well positioned to complete data entry and analysis as well as craft publications to disseminate these findings within our no cost 6 month extension.

REFERENCES: NA